

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

**1-109.** (canceled)

**110.** (Currently amended) A method for designing an oligonucleotide sequence having a selected duplex stability comprising:

a) providing an oligonucleotide having a sequence of N bases and N-1 neighboring base pairs, wherein said oligonucleotide comprises at least one modified base selected from the group consisting of a universal base, unsubstituted and 3-substituted pyrazolo[3,4-d]pyrimidines and 5-substituted pyrimidines; ~~and~~

b) calculating the duplex stability of said oligonucleotide using an algorithm applying a nearest-neighbor model for duplex formation thermodynamics for each of the N-1 neighboring base pairs, each nearest neighbor thermodynamic parameter defining a thermodynamic contribution of two corresponding neighboring bases, optionally repeating steps a)-b) to obtain a sequence having said selected duplex stability; and

c) outputting the sequence to a user or a display.

**111.** (Currently amended) A method for designing an oligonucleotide sequence having a selected duplex stability comprising:

a) providing an oligonucleotide having a sequence of N bases and N-1 neighboring base pairs, wherein said oligonucleotide comprises at least one modified base selected from the group consisting of a universal base, unsubstituted and 3-substituted pyrazolo[3,4-d]pyrimidines and 5-substituted pyrimidines; and a minor groove binder; ~~and~~

b) calculating a melting temperature ( $T_m$ ) of said oligonucleotide using an algorithm applying nearest neighbor thermodynamic parameters for each of the N-1 neighboring base pairs, each nearest neighbor thermodynamic parameter defining a thermodynamic

contribution of two corresponding neighboring bases, optionally repeating steps a)-b) to obtain a sequence having said selected duplex stability; and

c) outputting the sequence to a user or a display.

**112.** (Previously presented) The method of any one of claims **110** or **111**, wherein said oligonucleotide sequence is derived from a database source.

**113.** (Previously presented) The method of claim **112**, wherein said database source is GENBANK.

**114.** (Previously presented) The method of any one of claims **110** or **111**, wherein said at least one modified base is a member selected from the group consisting of a base attached to an amino acid, a polyamide nucleic acid (PNA) and a locked nucleic acid sugar.

**115.** (Previously presented) The method of claim **114**, wherein said modified base is attached to PNA.

**116.** (Previously presented) The method of claim **114**, wherein said modified base is attached to a locked nucleic acid sugar.

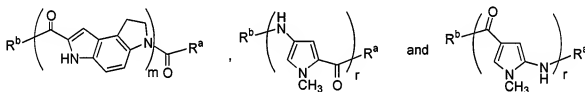
**117.** (Previously presented) The method of any one of claims **110** or **111**, wherein said oligonucleotide has an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.

**118.** (Previously presented) The method of any one of claims **110** or **111**, wherein said at least one modified base is a member selected from the group consisting of a universal base, PPA, PPG, PPPA, PPPG, PU, PC, HOPU, HOBuU, HOBuC, (NH<sub>2</sub>)<sub>2</sub>PPPA, (NH<sub>2</sub>)<sub>2</sub>PPPAOH, (NH<sub>2</sub>)<sub>2</sub>BuPPAOH, (NH<sub>2</sub>)<sub>2</sub>PPAI, and HOBuPPG.

**119.** (Previously presented) The method of claim **110**, wherein said oligonucleotide has attached to it one or more members selected from the group consisting of a minor groove binder, a fluorophore and a quencher.

**120.** (Previously presented) The method of claim **119**, wherein said oligonucleotide sequence has a minor groove binder attached thereto.

**121.** (Previously presented) The method of claim **111** or **120**, wherein said minor groove binder has a formula selected from the group consisting of:



wherein

the subscript  $m$  is an integer of from 2 to 5;

the subscript  $r$  is an integer of from 2 to 10; and

each  $R^a$  and  $R^b$  is independently a linking group to said modified oligonucleotide,  $H$ ,  $OR^c$ ,  $NR^dR^e$ ,  $COOR^c$  and  $-CONR^cR^d$  wherein each  $R^c$  and  $R^d$  is selected from the group consisting of  $H$ ,  $(C_1-C_{12})$ heteroalkyl,  $(C_2-C_{12})$ heteroalkenyl,  $(C_2-C_{12})$ heteroalkynyl,  $(C_1-C_{12})$ alkyl,  $(C_2-C_{12})$ alkenyl,  $(C_2-C_{12})$ alkynyl, aryl $(C_1-C_{12})$ alkyl and aryl.

**122.** (Previously presented) The method of claim **120**, wherein said minor groove binder is attached to the oligonucleotide via a quencher molecule.

**123.** (Previously presented) The method of any one of claims **110** or **111**, wherein said algorithm predicts the melting temperature ( $T_m$ ) of said oligonucleotide with an accuracy of about  $\pm 2^\circ C$ .

**124.** (Previously presented) The method of any one of claims **110** or **111**, wherein said method is applied to establish conditions for hybridization, renaturation, mapping

variations of base compositions of sequences or determination of sequence complexity and divergence.

**125.** (Previously presented) The method of any one of claims **110** or **111**, wherein said oligonucleotide is a capture probe in an array.

**126.** (Previously presented) The method of claim **115**, wherein said oligonucleotide an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.

**127.** (Previously presented) The method of claim **116**, wherein said oligonucleotide has an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.